REMARKS

Claims 19-33 are currently pending in the application. Claims 34-51 have been withdrawn without prejudice as being drawn to a nonelected invention, which can be prosecuted at a later date. Claims 20, 26, 30, 32, and 33 have been amended herein.

Claim 20 has been amended herein to indicate that the virus protein is from a virus selected from the enumerated group.

Dependent claims 26, 30, and 32 have been amended to be in independent form.

Claims 33 and 34 have been amended to better define the claimed embodiments of the invention.

Support for these amendments can be found throughout the specification and in the claims as originally filed.

Applicants respectfully submit that no new matter has been added by these amendments.

The Office Action states that the paper sequence listing as filed does not contain SEQ ID NO: 20, which is on the CRF. Applicants respectfully submit that the sequence listing filed November 29, 2001 contains SEQ ID NO: 20 (and SEQ ID NO:21). However, in order to expedite prosecution of this application, Applicants enclose herewith a complete paper copy of the sequence listing and computer readable form in accordance with the requirements of 37 C.F.R. § 1.825. Applicants have also amended the Sequence Listing submitted herewith to correct the description of SEQ ID NO:15. Support for this amendment can be found in the specification at page 11, paragraph 42. Accordingly, Applicants respectfully submit that no new matter has been added by this amendment.

Applicants assume that all rejections not restated herein have been withdrawn.

The outstanding rejections are addressed individually below.

1. Claims are definite under 35 U.S.C. § 112, second paragraph.

Claims 19-33 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for the recitation of certain terms described below. Applicants respectfully traverse this rejection in part.

a) "Derived"

The Office Action states that the rejection based on "derived" is maintained because the term "derived" is not used in the cited passage and the passage does not set forth the metes and bounds of "derived." (Office Action, page 4) Although Applicants do not agree with this rejection, in order to expedite the prosecution of this application, Applicants have amended claim 20 to recite that the virus protein is from a virus selected from the enumerated group.

Applicants respectfully submit that only claim 20 (and claim 21 dependent thereon) contains the term "derived." Therefore, Applicant respectfully submits that even without this amendment this rejection is moot as to claims 19 and 22-33.

Accordingly, Applicants respectfully submit that this rejection has been overcome, and thus should be reconsidered and withdrawn.

b) "Not expressing LHBs"

The Office Action states that claim 33 is also rejected because it is not clear what is "not expressing LHBs." (Office Action, page 6)

In order to expedite prosecution of this application, claim 33 has been amended to recite wherein the cells do not express LHBs as previously indicated in prior version of the claim.

Accordingly, Applicants respectfully submit that this rejection has been overcome, and as such request that this rejection be reconsidered and withdrawn.

2. ***Claims 19-25, 27-29, 31, and 33 comply with the written description requirement.***

Claims 19-25, 27-29, 31, and 33 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

The Office Action states that the term "cell permeability-mediating peptide" is at issue. The Office Action states that the "claims are drawn to a genus of peptides that are described by function" and that "Applicant has not disclosed a representative number of species to indicate possession of the full scope of the claimed genus . . . ." The Office Action concludes that "Applicant has not shown possession of the full range of peptides commensurate in scope of the claim to a genus." (Office Action, page 5)

M.P.E.P. § 2163 (I) states that to

> satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention[at the time the application was filed]. . . . Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" . . . or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

(Citations omitted.) M.P.E.P. § 2163 (I)(A) states that there "is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." Applicants submit that the term "cell permeability-mediating peptide" was present in the original claims as filed.

The Examiner directed Applicants to M.P.E.P. 2163 (II)(A)(3)(a)(ii) (For Each claim drawn to a genus). Applicants note that in addition to the section referred to by the Examiner, this section of the M.P.E.P. also states that there "may be situations where one species adequately supports a genus." Furthermore, M.P.E.P. § 2163 (II)(A)(2)

states that generally "there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification." M.P.E.P. § 2163 (III)(A) states that a *prima facie* case for lack of written description is established by "providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed."

Applicants respectfully submit that there is not a *prima facie* case for lack of written description. The specification provides a definition of the term "cell permeability-mediating peptide" at page 2, paragraph 7, which states that such a peptide includes "any peptides capable of mediating a cell permeability for substances, in particular proteins." The specification provides SEQ ID NO:20 as a nonlimiting example of such a cell permeability-mediating peptide. Furthermore, SEQ ID NO:1, which describes the amino acid sequence for a fusion protein, includes a similar cell permeability-mediating peptide sequence in which the "leucine" has been replaced by "isoleucine."

Furthermore, the specification indicates at page 4, paragraph 15 that the fusion protein can differ from the amino acid sequence of FIG. 2 by one or more amino acids. The term "an amino acid sequence differing in one or more amino acids" is defined at page 4, paragraph 16 as indicating that "this amino acid sequence specifies a fusion protein which has comparable elements and functions as the fusion protein in Fig. 1 or figure 2 but which differs from the amino acid sequence of Fig. 1 or Fig. 2 up to 20%, preferably 10%." In addition, Examples 1 and 2 at pages 9-12 demonstrate the preparation of a particle according to the claimed embodiments of the invention. As indicated at page 10, paragraph 37, the cell permeability-mediating peptide of Example 1 is in the LHBs (specifically the PreS2 region of the LHBs as mentioned at page 1, paragraph 5). As indicated at page 11, paragraph 42, the cell permeability-mediating

peptide of Example 2 is encoded by SEQ ID NO:15, which comprises SEQ ID NO:21, and is referred to as ZPP.

Additionally, Applicants enclose herewith copies of five references as nonlimiting examples that indicate that one of skill in the art at the time the application was filed would have recognized that the inventor was in possession of the invention as claimed. As discussed above, information which is well known in the art need not be described in detail in the specification.

Derossi, *et al.*, (1994) *Journal of Biological Chemistry* 269(14): 10444-10450 (attached hereto as Appendix A), teaches that "the homeodomain of Antennapedia (that we called pAntp) is capable of translocating across the neuronal membranes and is conveyed to the nuclei." (Derossi, *et al.*, page 10444) They demonstrate that "a 16-amino acid long peptide that corresponds to the third helix deleted of its N-terminal glutamate is capable of translocating through biological membranes." (Derossi, *et al.*, page 10444)

Rojas, *et al.*, (1998) *Nature Biotechnology* 16:370-375 (attached hereto as Appendix B), reports "a method to engineer proteins with cell-membrane permeability." (Abstract) This paper teaches "a simple way to generate various cell-permeable proteins, by which one can deliver proteins or protein domains of interest into living cells for functional characterization or regulation." (Rojas, *et al.*, page 374)

Vives, *et al.*, (1997) *Journal of Biological Chemistry* 272 (25):16010-16017 (attached hereto as Appendix C), teaches that "chemical coupling of a Tat-derived peptide (extending from residues 37 to 72) to several proteins allowed their functional internalization into several cell lines or tissues." (Abstract)

Elliott *et al.*, (1997) *Cell* 88:223-233 (attached hereto as Appendix D), teaches that "the HSV-1 structural protein VP22 has the remarkable property of intercellular transport, which is so efficient that following expression in a subpopulation the protein spreads to every cell in a monolayer, where it concentrates in the nucleus and binds chromatin." (Abstract) Elliott *et al.* also teaches that "VP22 can efficiently deliver

heterologous peptides into cells either after endogenous synthesis and transport, or by application to the medium and uptake." (Elliott *et al.*, page 229)

Phelan *et al.*, (1998) *Nature Biotechnology* 16:440-443 (attached hereto as Appendix E), also teaches that VP22 exhibits "the remarkable property of inter-cellular trafficking whereby the protein spreads from the cell in which it is synthesized to many surrounding cells" and provides results demonstrating "intracellular transport of large functional proteins." (Abstract)

Thus, at the time of the invention, various cell-permeability mediating peptides were known in the art.

Accordingly, Applicants respectfully submit that a person skilled in the art at the time the application was filed would have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed. Furthermore, one of skill in the art would have recognized that Applicants had more than one representative sequence for a cell permeability-mediating peptide in their possession at the time that the application was filed.

Therefore, Applicants submit that the term "cell permeability-mediating peptide" does not lack written description. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

3. ***Claims 19 and 20 are not anticipated under 35 U.S.C. § 102(b) by Rosenberg.***

Claims 19 and 20 stand rejected as allegedly being anticipated under 35 U.S.C. § 102(b) by Rosenberg (WO 97/24453). Applicants respectfully traverse this rejection.

M.P.E.P. § 2131 quotes that a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2121.01 quotes that in "determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an

'enabling disclosure'" and states that a "reference contains an 'enabling disclosure' if the public was in possession of the claimed invention before the date of invention." (citation omitted)

Claim 19 recites a particle comprising a protein envelope with a fusion protein, the fusion protein comprising a virus protein, a cell permeability-mediating peptide, and a heterologous cell-specific binding site, and with nucleic acid sequences present within the protein envelope, each of the nucleic acid sequences comprising a sequence encoding a virus-specific packaging signal and a sequence encoding a structural gene. Claim 20 recites various viruses that the virus protein can be from.

Although Applicants do not necessarily agree with the description of Rosenberg provided in the Office Action, Applicants note that in contrast to the cited claims, Rosenberg does not disclose a fusion protein comprising a virus protein, a cell permeability-mediating peptide, and a heterologous cell-specific binding site.

As discussed above, the specification provides a definition of the term "cell permeability-mediating peptide" at page 2, paragraph 7, which states that such a peptide includes "any peptides capable of mediating a cell permeability for substances, in particular proteins." The specification provides SEQ ID NO:20 as a nonlimiting example of such a cell permeability-mediating peptide. In addition, as discussed above with reference to Appendices A-E, various cell-permeability mediating peptides were known in the art at the time of the invention.

In contrast, Rosenberg states that "internalization of the virus" or "internalization of the particle" refers to "internalization of a virus or a particle or a vesicle into host cell by contact of a receptor on the cell surface with the ligand portion of the viral surface protein or by contact of the receptor on the cell surface with the ligand that is affixed to the particle. The virus or particle is then internalized after a binding pair is formed between the receptor and the ligand portion of either the viral surface protein or the altered particle, as the case may be." Applicants understand this

description as referring to receptor-mediated endocytosis. Applicants submit that the cell permeability mediated by the "cell permeability-mediating peptide" claimed in the instant application and discussed above is different from receptor-mediated endocytosis.

Accordingly, Applicants submit that Rosenberg does not disclose a fusion protein comprising a virus protein, a cell permeability-mediating peptide, and a heterologous cell-specific binding site.

Furthermore, Rosenberg does not disclose that the nucleic acid sequences present within the protein envelope comprise a sequence encoding a virus-specific packaging signal.

In addition, Rosenberg does not enable the claimed embodiments of the invention. The examples recited do not provide specific detail regarding how to perform the experiments to create the disclosed particles and chimeric proteins. Additionally, Rosenberg provides no working examples (either *in vitro* or *in vivo*) indicating that the polypeptides, particles or methods disclosed therein would work.

Therefore, Applicants submit that Rosenberg does not anticipate claims 19 and 20 under 35 U.S.C. § 102(b). Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

4. Claims 26, 30 and 32 should be indicated allowable.

Applicants note that due to the fact that the rejection under 35 U.S.C. § 112, second paragraph, based on the word "derived" is only applicable to claims 20 and 21, claims 26, 30 and 32 have no outstanding rejections. Accordingly, Applicants have rewritten these claims in independent form. Applicants respectfully submit that at least these claims are allowable.

CONCLUSIONS

In view of the arguments set forth above, Applicants respectfully submit that the rejections contained in the Office Action mailed on May 5, 2004, have been overcome, and that the claims are in condition for allowance.

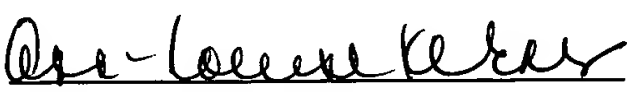
Applicants enclose a Petition for a One Month Extension of Time pursuant to 37 C.F.R. § 1.136, until September 7, 2004 (September 5, 2004 being a Sunday and September 6, 2004 being Labor Day), to respond to the Examiner's Office Action mailed on May 5, 2004. Please charge our Deposit Account No. 08-0219 the $110.00 fee for this purpose.

Applicants also enclose herewith a Supplemental Information Disclosure Statement. Please charge our Deposit Account No. 08-0219 the $180.00 fee for this submission.

No other fees are believed to be due in connection with this response. However, please charge any underpayments or credit any overpayments to Deposit Account No. 08-0219.

If the Examiner believes that any further discussion of this communication would be helpful, please contact the undersigned at the telephone number provided below.

Respectfully submitted,



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